ISIS-4789 PATENT

(250 ml) is added DMT-Cl (3.3 g). The reaction is stirred for 16 hours. The reaction is added to ice/water/ethyl acetate, the organic layer separated, dried, and concentrated *in vacuo* and the resultant gum chromatographed on silica gel (ethyl acetate-methanol triethylamine) to give the title compound.

EXAMPLE 24

 $3'-O-[Propyl-(3-phthalimido)]-5'-O-DMT-N6-Benzoyl-adenosine-2'-O-(2-cyanoethyl-N,N-diisopropyl)\ phosphoramidite$

[0161] 3'-O-(Propyl-3-phthalimide)-5'-O-DMT-N⁶-benzoyladenosine is treated with (β-cyanoethoxy)chloro-N,N-diisopropyl)aminophosphane in a manner similar to the procedure of Seėla, et al., Biochemistry 1987, 26, 2233. Chromatography on silica gel (EtOAc/hexane) gives the title compound as a white foam.

EXAMPLE 25

3'-O-(Aminopropyl)-adenosine

[0162] A solution of 3'-O-(propyl-3-phthalimide)adenosine (8.8 g, 19 mmol), 95% ethanol (400 mL) and hydrazine (10 mL, 32 mmol) is stirred for 16 hrs at room temperature. The reaction mixture is filtered and filtrate concentrated *in vacuo*. Water (150 mL) is added and acidified with acetic acid to pH 5.0. The aqueous solution is extracted with EtOAc (2 x 30 mL) and the aqueous phase is concentrated *in vacuo* to afford the title compound as a HOAc salt.

ISIS-4789 PATENT

EXAMPLE 26

3'-O-[3-(N-trifluoroacetamido)propyl]-adenosine

[0163] A solution of 3'-O-(propylamino)adenosine in methanol (50 mL) and triethylamine (15 mL, 108 mmol) is treated with ethyl trifluoroacetate (18 mL, 151 mmol). The reaction is stirred for 16 hrs and then concentrated *in vacuo* and the resultant gum chromatographed on silica gel (9/1, EtOAc/MeOH) to give the title compound.

EXAMPLE 27

N6-Dibenzoyl-3'-O-[3-(N-trifluoroacetamido)propyl]-adenosine

[0164] 3'-O-[3-(N-trifluoroacetamido)propyl]adenosine is treated as per Example 22 using a Jones modification wherein tetrabutylammonium fluoride is utilized in place of ammonia hydroxide in the work up. The crude product is purified using silica gel chromatography (EtOAc/MeOH 1/1) to give the title compound.

EXAMPLE 28

N6-Dibenzoyl-5'-O-DMT-3'-O-[3-(N-trifluoroacetamido)propyl]-adenosine

[0165] DMT-Ci (3.6 g, 10.0 mmol) is added to a solution of N⁶-(dibenzoyl)-3'-O-[3-(N-trifluoro-acetamido)propyl)adenosine in pyridine (100 mL) at room temperature and stirred for 16 hrs. The solution is concentrated *in vacuo* and chromatographed on silica gel (EtOAc/TEA 99/1) to give the title compound.

ISIS-4789 PATENT

EXAMPLE 29

N6-Dibenzoyl-5'-O-DMT-3'-O-[3-(N-trifluoroacetamido)propyl]-adenosine-2'-O-(2-cvanoethyl-N.N-diisopropyl) phosphoramidite

[0166] A solution of N⁶-(dibenzoyl)-5'-O-(DMT)-3'-O-[3-(N-trifluoroacetamido)propyl]adenosine in dry CH₂Cl₂ is treated with bis-N,N-diisopropylamino cyanoethyl phosphite (1.1 eqiv)
and N,N-diisopropylaminotetrazolide (catalytic amount) at room temperature for 16 hrs. The
reaction is concentrated *in vacuo* and chromatographed on silica gel (EtOAc/hexane/TEA 6/4/1) to
give the title compound.

EXAMPLE 30

3'-O-(butylphthalimido)-adenosine

[0167] The title compound is prepared as per Example 21, using N-(4-bromobutyl)phthalimide in place of the 1-bromopropane. Chromatography on silica gel (EtOAC-MeOH) gives the title compound. ¹H NMR (200 MHZ, DMSO-4₆) δ 5.88 (d, 1H, C₁H).

EXAMPLE 31

N6-Benzoyl-3'-O-(butylphthalimido)-adenosine

[0168] Benzoylation of 3'-O-(butylphthalimide)adenosine as per Example 22 gives the title compound.